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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,563	04/16/2004	Mark A. Hoffman	CRNI.114071	2108

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EXAMINER	
SIMS, JASON M	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/826,563	HOFFMAN ET AL.	
	Examiner	Art Unit	
	JASON SIMS	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-8,10,12-15,17 and 19-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-8,10,12-15,17 and 19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/14/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/14/2010 has been entered.

Applicant's arguments, filed 12/14/2010, have been fully considered. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicants have amended their claims, filed 12/14/2010, and therefore rejections newly made in the instant office action have been necessitated by amendment.

Claims 1, 3, 5-8, 10, 12-15, 17, and 19-23 are the current claims hereby under examination.

The following rejection has been modified, which was necessitated by amendment:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 5-8, 10, 12-15, 17 and 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over ICHIKAWA (Internal Medicine (July, 2000) vol. 39, no. 7, pp. 523-524) (This reference has been submitted via IDS filed on 4/11/2008 and therefore will not be cited on a separate 892 form) in view REINHOFF et al. (US 2002/0049772 A1, filed 5/26/2000), in view of Fey et al. (US A/N 2002/0038227), and further in view of Fiedotin et al. (US P/N 7,509,263) and further in view of Hogan (US P/N 2002/0110823 with a priority date of 7/11/2000).

The claims are drawn to a computer system, computer readable medium and a method in a computer system for generating an output including information regarding the likelihood a person has a gene variant indicative of an atypical event, comprising the steps of:

a) displaying a first user interface to a clinician, the user interface configured to display and receive clinical agent information including at least one identifier of a clinical agent;

b) receiving from the user interface the clinician's inputs including at least one identifier of a clinical agent and a dosage of the clinical agent, wherein receiving includes receiving a selection of an entry in a listing of clinical agents on the first user interface and a selection of the dosage from a range of dosages recommended for the clinical agent associated with the selected entry;

c) accessing a data structure to determine if a gene variant is known to be associated with one or more atypical events for the identifier of the clinical agent

received from the clinician, wherein the data structure includes an agent-gene association table;

d) inquiring if the person to whom the clinical agent is to be administered has a stored genetic test result value for the gene variant, wherein inquiring includes accessing an electronic medical record (EMR) of the person;

e) accessing hereditary information for the person if the person does not have a genetic test result value for the genetic variant, the hereditary information being information that may be utilized to determine if the person has a predisposition for certain conditions, wherein the hereditary information is obtained from the EMR of the person;

f) utilizing the hereditary information for the person to determine the likelihood the person has the gene variant; and

g) generating an output including information regarding the likelihood a person has a gene variant indicative of an atypical event based on hereditary information; and

h) displaying a second user interface to the clinician, the user interface configured to display the output regarding the likelihood the person has the gene variant indicative of an atypical event for the identifier of the clinical agent received from the clinician.

i) determining a first risk of damage to the person, the first risk of damage being associated with administering to the person the dosage of the clinical agent as indicated by the clinician;

j) determining a second risk of damage to the person, the second risk of damage being associated with the damage to the person by not administering the dosage of the clinical agent;

k) utilizing the first risk of damage and second risk of damage determinations to generate an output including an automated clinical response containing suggestions for clinical actions to be taken by the clinician, and

l) displaying a third user interface to the clinician, the user interface configured to display the output regarding the generated automated clinical response.

With regards to limitations of claims 1, 8 and 15: ICHIKAWA teaches at page 523, first column, 2nd and 3rd paragraphs data related to azathioprine or mercaptopurine (clinical agents), which reads on a limitation of step b) of clinical agent information, the clinical agent information including an identifier of the agent. ICHIKAWA at page 523, 3rd and 4th paragraphs, teaches about thiopurine S-methyl transferase (TPMT), which has genetic polymorphisms associated with one or more atypical events for the clinical agents, which reads on limitations of step c) accessing a data structure to determine if a gene variant is known to be associated with one or more atypical events for the clinical agent information. ICHIKAWA at page 523, first column, last 5 lines, teaches it is quite important to know in advance whether a patient who will be treated with thiopurine derivitives, has genetic polymorphism at TPMT sites, which reads on limitations of step d) inquiring if the person has a stored genetic test result value for the gene variant.

ICHIKAWA at page 523, second column, first paragraph teaches a method for processing hereditary (genetic) information related to response to azathioprine or mercaptopurine (clinical agents) wherein genetic tests results for individual patients are accessed, which reads on limitations of step e) accessing hereditary information for the person if the person does not have a genetic test result value for the genetic variant. ICHIKAWA further teaches at page 523, first column, last paragraph and second column first paragraph that the presence of a polymorphism is then determined, wherein particular mutations or polymorphisms are associated with atypical clinical events (side effects) of administration of various drugs, and a decision made to change a drug dosage, which reads on step f) utilizing the hereditary information for the person to determine the likelihood the person has the gene variant. Since drug dosages are based on the genetic testing results in the method of ICHIKAWA, the method necessarily includes a step of outputting the test results, which reads on step g) generating an output including information regarding the likelihood a person has a gene variant indicative of an atypical event based on hereditary information.

ICHIKAWA does not explicitly teach the computer aspect of accessing a data structure as in a limitation of step b), or the computer implemented aspects of the instant steps.

Rienhoff et al. at the abstract, teach a computer program product that allows identification of a susceptibility locus in individuals using genetic screening methods to assess their risk of certain diseases wherein the information can be used to gauge drug responses.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the computer implemented methods for allowing identification of a susceptibility locus in individuals using genetic screening methods to assess their risk of certain diseases wherein the information can be used to gauge drug responses as taught by Rienhoff et al. to identify individuals with genetic polymorphisms of TPMT sites prior to the administration of the clinical agents. This is because ICHIKAWA at page 524, states that it would be possible to anticipate the effectiveness and side effects of all drugs, not after the administration of the drugs, but in advance based on the information of genetic polymorphism. Furthermore, the automation of such a method as taught by Rienhoff et al. would have been obvious because it would increase efficiency of testing and data management. Therefore, to use the computer program product taught by Rienhoff et al. to automate the method taught by ICHIKAWA, one of ordinary skill in the art would have recognized that applying the known technique would have yielded predictable results and resulted in an improved method.

Ichikawa and Rienhoff et al. suggest, but do not explicitly teach displaying a first user interface to a clinician, the user interface configured to display and receive clinical agent information including at least one identifier of a clinical agent as in step a) and displaying a second user interface to the clinician configured to display the output as in step g).

Fey et al. teach at paragraphs [0022] [0048] and [0055] an application of health data management which involves a graphical user interface written for web browser applications wherein the user has a unique identification and may enter information

through the GUI. Fey et al. at paragraph [0012] teach keeping secure health records, which are accessible by authorized health persons. Fey et al. further teach that custom reports are generated at the time tests are performed that explains the results. Fey et al. teach at paragraph [0022] wherein results are prepared for the individual and physician. Fey et al. teach at paragraph [0047] wherein the health data may be used by doctors. In addition, Fey et al. at paragraphs [0053] – [0059] and [0063] – [0075] teach a system comprising a means, i.e. a displaying component and computer storage media configured for displaying a graphical user interface. With further regards to claim 23, Fey et al. teach at paragraph [0031] storing the genetic test results.

Fey et al. does not explicitly teach a GUI that is configured to solicit input from a clinician to ascertain an identifier of a clinical agent as in step b) or whether to authorize performing a genetic test on a patient. In fact, Fey et al. teach, i.e. paragraph [0057] that the invention is directed to enabling a client/consumer to order genetic testing without doctor's approval. Furthermore, Fey et al. teach that a client can use the taught invention to determine genetic risk towards disease or conditions or discover genetic predispositions.

It is noted that the functionality of Fey's system, not the method steps, is what is relied upon in the instant rejection. The invention taught by Fey et al. has the functionality of using a graphical user interface to solicit input, albeit from a client, to ascertain whether to perform a genetic test, displays identification of the genetic test to be performed, receives approval or authorization from the client to carry out the genetic

test, ensures identification of the person, and is configured to receive result value of the genetic test for the person.

Fiedotin et al. at the abstract, Fig. 3a-4d, col. 6, lines 45-54, col. 12, lines 64-67 and col. 13, lines 1-6 teach various graphical user interfaces for displaying clinical agent information, warnings about contraindications or adverse reactions and other information.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used a system for displaying information and receiving clinician input as taught as taught by Fey et al. and Fiedotin et al. for use in the invention taught by Ichikawa and REINHOFF. This is because the use of graphical user interfaces for displaying information or receiving clinician input as taught by Fey et al. and Fiedotin et al. for use in known methods as taught by Ichikawa and REINHOFF is seen as the automation of known methods. Automation of known methods is an obvious step or improvement because the automation, i.e. use of computers, to perform otherwise known methods is not an unobvious variation from the teachings of prior art wherein automation was not performed. In other words, broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art (see In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958)). Furthermore, one of ordinary skill in the art could have applied the known improvements, i.e. the use of graphical user interfaces in known methods and the results would have been predictable to one of ordinary skill in the art. Moreover, a skilled artisan would find that the differences between the claimed invention

and the prior art were encompassed in known variations or in a principal known in the prior art.

The combination of Ichikawa, REINHOFF, Fey et al., and Fiedotin et al. do not explicitly teach an agent-gene association table or the risk associated with not administering the dosage of the clinical agent.

Hogan at Fig. 4 teaches an agent-gene association table. In addition, Hogan at the abstract teaches screening patients for markers indicative of responses to drugs and treatments to tailor a subject's medical or surgical treatment to reflect genetic information. Hogan teach at paragraphs [0015] – [0019], [0030], [0032], and [0035] – [0037] using a genomic profile for determining a medical treatment course of action, which includes before, during and following a medical procedure. Hogan describes how the information is used to generate a risk involved based on the information, such as a subject's prognosis, and odds of survival. It is inherent in the doctors decision tree to assess risk based on administering a particular drug and/or not administering a risk. The automation of that decision tree and/or and automated manual procedure for reflecting said decision tree is not an unobvious patentable distinction from what is routine. Furthermore, Hogan at paragraph [0126] describes the risk analysis for a doctor during a surgical procedure, wherein "the practitioner may choose an alternative drug." The fact that the doctor "may" choose an alternative drug carries the meaning of an inherent decision tree weighing the pros and cons to or not to administer a drug. In addition, Hogan at paragraphs [0186] - [0190] describe the automated computer means for utilizing the genomic profile data for a clinician, wherein the data is in the form of a

risk assessment for various treatment options the clinician may use or as recommendations for particular treatment options to "optimize the perioperative care of the subject." When a doctor receives treatment options wherein one of the options is selected and the others are not selected, this is an inherent form of assessing the risk of not administering the non-selected treatment options.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used an agent-gene association table and risk assessment for or not for administering a clinical agent such as that taught by Hogan for use in the method for displaying information on one or more user interfaces regarding the likelihood a person has a gene variant indicative of an atypical event as taught by the combination of Ichikawa, REINHOFF, Fey et al., and Fiedotin et al. This is because Ichikawa also teach the benefit of having this information in order to tailor treatments to a patient's genomic profile. Therefore, the known technique of determining using agent-gene association information along with a patient's genomic profile was recognized as part of the ordinary capabilities of one skilled in the art. One of ordinary skill in the art would have been capable of applying this known technique to the taught method and the results would have been predictable to one of ordinary skill in the art.

ICHIKAWA also teaches at page 523, second column, paragraphs 1 and 2, wherein the hereditary information includes ethnicities as in claims 3, 10, and 17.

Rienhoff et al. at paragraphs [0006]-[0007] teach the use of comprehensive medical databases for storing hereditary information. Furthermore, Rienhoff et al. at paragraph [0011]-[0012] teach determining, storing, and comparing polymorphic

genomic profiles of individuals in databases wherein these databases are used to assist in performing clinical trials and drug administration (see paragraph [0014]), which reads on a broad interpretation of a comprehensive healthcare system as in claims 5, 12, and 19.

Reinhoff et al. at paragraph [0010] teach a computer program that allows identification of a susceptibility locus in individuals using genetic screening methods to assess individuals' risk of certain diseases. Reinhoff et al. at paragraph [0011] teach determining a statistically significant difference between the polymorphic profiles for each individual of the population and separating the population into a first subpopulation and a second subpopulation based up the profiles. Reinhoff et al. teach at paragraph [0014] wherein databases may be updated and expanded. Moreover, Reinhoff et al. at paragraph [0027] teach how an individual's polymorphic profile can be ordered and stored, which reads on claims 6, 13, and 20 and limitations of claims 7,14, and 21.

Fiedotin et al. at the abstract, Fig. 3a-4d, col. 6, lines 45-54, col. 12, lines 64-67 and col. 13, lines 1-6 teach various graphical user interfaces for displaying clinical agent information, warnings about contraindications or adverse reactions and other information, such as other alternative drugs in the same class that may be used, which reads on the other limitations of claims 7, 14, and 21.

REINHOFF teach at paragraph [0076] claim 22.

Response to Arguments

Applicant's arguments filed 12/14/2010 have been fully considered but they are not persuasive.

Applicant at pages 11-13 summarize specific necessities that are to accompany a rejection of claims under 35 USC 103. Applicant at pages 14-19 reiterate the amended claims 1,8, and 15 and summarize the amendments attempted to overcome the prior art of record.

Applicant at page 19 of the remarks argues that each of the references fails to teach or suggest a first risk of damage to a patient, where the first risk is associated with administering to the person the dosage of the clinical agent as indicated by the clinician and determining a second risk of damage to the person that is associated with the damage caused to the person by not administering the dosage of the clinical agent.

Applicant's arguments are not found persuasive. With regards to the first allegation that the combined references do not teach or suggest determining a first risk of damage to the person associated with administering the dosage of the clinical agent, each of the references Ichikawa, REINHOFF, and Hogan teach determining a risk associated with a drug dosage, see for example Hogan at paragraph [0008]. With regards to the second risk, which is directed to not administering a dosage, Hogan teach at paragraphs [0015] – [0019], [0030], [0032], and [0035] – [0037] using a genomic profile for determining a medical treatment course of action, which includes before, during and following a medical procedure. Hogan describes how the information is used to generate a risk involved based on the information, such as a subject's prognosis, and odds of survival. It is inherent in the doctors decision tree to assess risk based on administering a particular drug and/or not administering a risk. The automation of that decision tree and/or and automated manual procedure for

reflecting said decision tree is not an unobvious patentable distinction from what is routine. Furthermore, Hogan at paragraph [0126] describes the risk analysis for a doctor during a surgical procedure, wherein "the practitioner may choose an alternative drug." The fact that the doctor "may" choose an alternative drug carries the meaning of an inherent decision tree weighing the pros and cons to or not to administer a drug. In addition, Hogan at paragraphs [0186] - [0190] describe the automated computer means for utilizing the genomic profile data for a clinician, wherein the data is in the form of a risk assessment for various treatment options the clinician may use or as recommendations for particular treatment options to "optimize the perioperative care of the subject." When a doctor receives treatment options wherein one of the options is selected and the others are not selected, this is an inherent form of assessing the risk of not administering the non-selected treatment options.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jason Sims, whose telephone number is (571)-272-7540.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Marjorie Moran can be reached via telephone (571)-272-0720.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61

(November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/ Jason Sims /

Claim Rejections - 35 USC § 103-Modified/Maintained

The following rejection has been modified/necessitated by amendment:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6, 11-14, 16, 18, 20-23, 27-31, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hogan (US A/N 2002/0110823) in view of Portwood et al. (US P/N 5,950,630) in view of Markin (US P/N 5,985,670) and further in view of Fey et al. (US 2002/0052761).

The claims are directed to a computer-implemented method for displaying a warning that a clinical agent received from a clinician should not be administered to a person, comprising the steps of:

Initially receiving from a clinician clinical agent information, the clinical agent information including an identifier of a specific clinical agent and a dosage of the specific clinical agent, wherein receiving includes receiving a selection of an entry in a listing of clinical agents on a graphical user interface and a selection of the dosage from a range of dosages recommended for the clinical agent associated with the selected entry;

identifying each of the genes associated with the clinical agent by comparing the identifier of the clinical agent received from the clinician to a first data set containing agent-gene associations, wherein the associated genes are likely to interact with the clinical agent to result in an atypical event;

when a gene is associated with the clinical agent, automatically obtaining a genetic test result value for the associated gene of the person, wherein

automatically obtaining comprises:

(a) receiving identification of the person to whom the clinical agent is to be administered and proper authorization to access an electronic medical record (EMR) of the person; and

(b) utilizing identfication and the proper authorization to access patient information within the EMR of the person stored within a comprehensive healthcare system;

when the patient information comprises the genetic test result value for the associated gene of a person, comparing the genetic test result value to a second data set containing one or more polymorphism values associated with one or more polymorphism values with one or more atypical clinical events for the clinical agent;

otherwise, performing the following procedure;

(a) seeking a clinician's authorization for a test by presenting a genetic test ordering window; and

(b) automatically ordering the test to determine the genetic test result value for the authorization is granted by a clinician at the genetic test ordering window;

determining whether the genetic test result value correlates to one or more of the one or more polymorphism values contained in the second data set; and

when the genetic test result value correlates to one or more of the one or more polymorphism values, displaying a warning to the clinician agent received from the clinician should not be administered, and recording an indication of the warning in the EMR of the person.

Hogan teaches limitations of claims 1, 18 and 35 as follows: Hogan at the abstract discusses a method for tailoring a subject's surgical treatment to reflect genetic information. Hogan at paragraph [0005] discusses that the choice of anesthetic

regimen, agent, and dose depends on the type of surgery or procedure. Therefore, it is implied that with planning a surgery a clinician will plan for the appropriate clinical agent, i.e. anesthesia drug, to be administered during the surgery, which reads on the first method step, receiving from a clinician, clinical agent information, the clinical agent information including an identifier of a specific clinical agent. Hogan at paragraphs [0007] – [0009] discusses how certain genes are associated with particular anesthetic drugs. Hogan at Figs. 4 and 5 describes data sets that comprise genes, alleles and associations with particular clinical agents. Therefore, it is implied that when determining if a gene is associated with a particular clinical agent that it is through comparing the identifier of the clinical agent to a data set comprising agent-gene associations. Hogan paragraphs [0011] – [0013] discusses genomic screening of a subject prior to or during a surgical procedure to obtain a genomic profile, which reads on the second step of determining if a gene is associated with the clinical agent by comparing the identifier of the clinical agent received from the clinician to a first data set containing agent-gene associations, and if a gene is associated with the clinical agent, obtaining a genetic test result value for the associated gene of the person. Hogan at paragraphs [0019] – [0022] discusses obtaining a genomic profile for a subject which screens the subject for one or more polymorphism values associated with one or more clinical events associated with one or more clinical agents. It is implied that the genomic profile result values are compared with a data set comprised of genes and alleles associated with clinical agents and events, such as in Figs. 4 and 5, which reads on the third method step comparing the genetic test result value to a second data set

containing one or more polymorphism values associated with one or more polymorphism values with one or more atypical clinical events for the clinical agent. Hogan at paragraphs [0018] and [0019] discusses screening a patient to determine a risk for surgical complications associated with known genetic variations. Furthermore, Hogan at paragraph [0190] discusses that the risk assessment for the various treatment options are displayed to the clinician on a computer monitor, which reads on the final method step of determining whether the genetic test result value correlates to one or more of the one or more polymorphism values contained in the second data set, and if so, displaying a warning to the clinician agent received from the clinician should not be administered. Moreover, Hogan at paragraphs [0189] – [0193] discusses the use of computers for performing the instant invention, all of which imply the use of computer programs and components for performing the instant method steps as in claim 18.

With respect to claim 1: Hogan suggests, but does not explicitly teach the step of automatically obtaining data of claim 1, wherein the step comprises:

Administering a test to gather a genetic test result only after steps (a)-(d) are met. In particular, Hogan do not explicitly teach first determining that patient information in an EMR does not comprise a genetic test result value for the associated gene.

Hogan suggests this because at paragraphs [0187] – [0195], Hogan teaches that a central processing facility where the genomic profiling data is stored provides the advantage of privacy, wherein privacy implies security and authorized access to data. Hogan further teaches specifically at paragraph [0193] that the subject, i.e. patient, can

determine the fate of the genomic profiling data. Furthermore, Hogan teaches at paragraph [0187] conditions for performing genomic profiling on a patient, wherein a patient would need to provide a genomic sample, which implies a patient giving an identifier, i.e. their name, and permission for a sample. In addition, Hogan at paragraph [0187] teaches information generated by perioperative genomic profiling is automated. Therefore, Hogan discusses the automation of processing information and the use of genomic profiling for determining or influencing a surgical plan.

In addition, Hogan suggest this because at paragraph [0187] they teach a set of criteria to be met prior to administering a genetic test or genomic profile test, such as whether the subject is a candidate for genomic profiling, if a particular method is available for performing said test, if the method will provide useful information for a particular application and its practicality, and if there is clinical utility, i.e. provide a predication of a phenotype related to the genotype, which read on steps (a), (c), and (d). In addition, Hogan at paragraphs [0192] - [0193] teach that the data may be stored for future use and thus if the data is stored for future use, it implies that a clinician may access this data prior to performing the genomic profile test.

It would have been obvious to one of ordinary skill in the art at the time of the invention to have first determined if the patient information comprises a genetic test result value for an associated gene in the method which has a list of criteria to be met prior to performing a genomic profiling test taught by Hogan. This is because Hogan teaches an invention for using a patient's genomic profile to provide the best surgical plan, which includes administration of an anesthetic drug, wherein a test result may

influence the surgical plan. Genomic profiling can be an expensive test as discussed by Hogan. Therefore, one of ordinary skill in the art could have pursued known potential solutions, i.e. automating a method of first checking a patient's medical record to first see if a genomic profile has been performed, with a reasonable expectation of success. One of ordinary skill in the art could have applied the known technique in the same way to the "base" method and the results would have been predictable, i.e. more cost effective in the case where a genomic profile had already been made. Hogan at the background and paragraphs [0030] – [0034] discuss the cost-effectiveness and importance of cost when performing perioperative testing of patients.

This is further obvious because Hogan teach a list of criteria that ensure the necessity, practicality, and utility of performing such a test. Thus, with such criteria being important prior to running such a test, it would have been obvious to also first determine if a genetic test result value exists in the current medical record of a patient prior to running said test. This obvious step would have been a design incentive which would have prompted one of ordinary skill in the art to vary the prior art in a predictable manner to result in the claimed invention.

Hogan suggests, but does not explicitly teach wherein receiving includes receiving a selection of an entry in a listing of clinical agents on a graphical user interface and a selection of the dosage from a range of dosages recommended for the clinical agent associated with the selected entry.

Hogan suggests this because paragraph [0005] describes that the choice of anesthetic regimen, agent and dose depends on the type of surgery or procedure, or

other medications, and any underlying diseases or pre-dispositions that a patient may have. Therefore, Hogan recognizes that particular agents and/or anesthetics have particular dose ranges, wherein the dose depends on those cited by Hogan.

Portwood et al. teach at the abstract an invention drawn towards a computer system for improving medical regimes, wherein data prescribed is compared to pharmaceutical data to verify acceptable limits, durations and check for contraindications and/or abnormalities. Portwood et al. further at claim 17 describe the system as comprising pharmaceutical data, which includes recommended dosage ranges for drugs in the pharmaceutical data and transmitting the determined dosages to a reporting unit, i.e. a display for a user.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used the pharmaceutical data which includes a listing of agents and recommended doses comprising a reporting unit to communicate the information to a user as taught by Portwood et al. in the method of genomic screening as taught by Hogan. This is because the invention of Hogan is directed to tailoring a subject's medical treatment whereas the invention taught by Portwood et al. is also directed towards improving medical regimes. Therefore, one of ordinary skill in the art could have applied the known system taught by Portwood et al. to the system taught by Hogan and the results would have been predictable. The system and pharmaceutical data described by Portwood et al. would have enabled a practitioner of the method taught by Hogan to have more efficient access to the pharmaceutical data that may be

used in tailoring the patient's medical regime, thus obviating the use of the invention taught by Portwood et al. in the method of Hogan.

The combination of Hogan and Portwood et al. do not explicitly teach seeking a clinician's authorization for a test by presenting a genetic test ordering window; and automatically ordering the test when authorization is granted by a clinician at the genetic test ordering window.

Markin teach at the abstract teach a system for the automatic testing of a laboratory specimen for use in a hospital setting. Markin teach at col. 3, lines 1-19 wherein the computerized system enables a doctor to enter a request for a specific test to be performed, i.e. seek and give authorization through a user interface, and the test is automatically ordered based upon the authorization.

Fey et al. teach at paragraphs [0006], [0050], and [0057] a graphical user interface designed for ordering genetic tests.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used a graphical user interface (GUI) for ordering genetic tests as taught by Fey et al. to automate ordering of tests taught by Markin and for use in the method of performing genomic screening and improving medical regimes as taught in the combination of Hogan and Portwood et al. This is because one of ordinary skill in the art would have recognized that applying the known technique of creating GUIs for automated ordering of tests to the method taught by Hogan and Portwood et al. would have yielded predictable results and resulted in an improved method.

With regards to the amendments of claim 18, Hogan suggests, but does not explicitly teach "when the clinical agent is not associated with a gene from the first data set, the first determining component approves administration of the clinical agent."

Hogan suggests this because Hogan at paragraphs [0030] – [0034] discuss the cost-effectiveness of performing perioperative tests, i.e. genomic profiling. Furthermore, at paragraphs [0119] – [0127] Hogan teaches that only markers that correlate with a subject's response or ones that can provide effective and helpful information are included in obtaining a genomic profile.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to have approved the administration of a clinical agent if the agent is not associated with a gene from a data set known to be associated with the agent. This is because Hogan teaches the need to perform effective testing wherein only markers for which a lot of data is available and known are selected. Hogan further teaches, such as at paragraph [0129] that markers may be subtracted from screening, which are known to not influence the patient. Thus it is implied from the teaching of Hogan, that if an agent is not associated with a gene from a known data set, that the administration of the agent would be approved. The invention of Hogan teaches to screen in a cost-effective way for approvable agents for administration. Hogan further teaches using markers for which a lot of data is known. Therefore, if no known gene was associated with an agent, it would be implied that the agent would be approved from the teachings of Hogan. A person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp, which would lead to the

anticipated success, thus the amended step is the product not of innovation, but of ordinary skill and common sense.

Hogan at paragraphs [0005], [0008], and [0138] discusses assessing the dosages associated with the clinical agents and risk assessments as in claims 2, and 19.

Hogan at paragraphs [0186] and [0188] – [0193] discusses that the clinical agent and genetic information may be stored and communicated via various computerized applications, including electronic medical records including computers, which reads on claims 3, 10, 20, and 27.

Hogan at paragraph [0031] – [0033] discusses a problem is "how to alter treatment course of action in response to results," as in genomic screening results and the present invention unites "medicine with genetics" to solve the described problem and to individualize treatment options for each subject. The genomic screening and obtaining genomic profiles and Figs. 4 and 5 disclosed as examples of data sets comprising gene and allele associations with clinical agents implies a querying to determine if a gene is associated with a planned-to-be-administered clinical agent as in claims 4, 5, 21, and 22.

Hogan at paragraphs [0190] – [0191] teaches outputting information about the atypical clinical event associated with the polymorphism values such that a "clinical action" may be initiated as recited in claims 6, 13, and 23.

Hogan at paragraph [0190] discusses that the risk assessment for the various treatment options are displayed to the clinician on a computer monitor, which reads on a warning that particular agents should not be administered as in claim 7.

Hogan at Fig. 4, discloses an example of a data set which includes information about risks associated with the atypical clinical events. Furthermore, paragraphs [0115], [0129], [0136] – [0147], and [0186] teaches comparing genetic test result values for multiple genes to polymorphism values associated with adverse reactions, i.e. risks associated with atypical clinical events, and that agent information may include dosage and other PK/PD parameters as in claims 12, 13, 16, 29, 30, and 33.

Hogan does not explicitly teach a method wherein the data sets of agent-gene associations may be updated as in claims 11 and 28.

Hogan at Fig. 2 describes in the analysis step of comparing genomic profile values to gene-agent association data that research data may be included in a data set used for comparison.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use data sets that may be updated. This is because it is a goal of Hogan's invention to tailor surgery treatments to subjects using genomic profiles and data, wherein it is implied that using the most updated genomic data available causes the instant invention to be used in its most opportunistic way. Therefore, it is implied that the gene-agent association data sets used are data sets that are updated as is also the nature of research, to update the current information existing in the field.

Hogan does not explicitly teach a method wherein the data sets are incorporated into a single data set as in claims 14 and 31.

However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used combined data sets in the method of Hogan as it can be a more efficient means for comparing data and easier for visually comparing or looking up information such as gene-agent information. Furthermore, it is a common goal of researchers to consolidate the most updated information into single sources of data, wherein combining the most up to date information on gene-agent associations into a single source such as a single data set would be in line with research goals. Therefore, using a single source of data such as a single data set would be more efficient for determining risk assessments based on gene-agent associations.

Response to Arguments

Applicant's arguments filed 2/26/2010 have been fully considered but they are not persuasive.

Applicant argues at page 16 of the remarks that the Hogan reference does not consider using a specific clinical agent and a particular dosage to begin the process of determining whether problematic interactions exist.

Applicant's arguments are not found persuasive because Hogan does look at what clinical agent, i.e. anesthesia, along with what dose is to be used with a particular surgical procedure. When this is known, Hogan then looks at the potential genomic profile of the patient to determine potential problematic interactions.

Applicant further argues that Hogan does not consider a GUI with the format indicated in claim 1 as amended.

Applicant's arguments are not found persuasive because Hogan is not used alone, but in combination with Portwood et al. (US P/N 5,950,630) in view of Markin (US P/N 5,985,670) and further in view of Fey et al. (US 2002/0052761) to teach the GUI as recited in said amended claims.

Applicant further argues that Hogan reference does not describe administering a test on the patient to gather a genetic test result value only after the criteria (a) – (d) have been met, but instead initially applies an assay to the tissue sample to generate a genomic profile without explicit consideration of whether a particular gene is associated with a clinical agent involved in a medical record.

Applicant's arguments are not found persuasive as applicant's recited claims do not necessitate that the steps be carried out in a particular order. Furthermore, the Hogan reference is not argued alone in teaching the recited claim amendments/limitations, but is used in combination of Markin, Fey et al., and Portwood et al., see the rejection stated above in the instant Office Action.

Applicant further argues that the Hogan reference does not explicitly teach the four criteria for administering a test to gather a genetic test result value.

Applicant's arguments are not found persuasive as it is the combination of Hogan, Markin, Fey et al., and Portwood that teach the four criteria recited in the claim limitations.

Applicant further argues at page 19 of the remarks that Hogan does not consider the specific risk-analysis as recited in amended claim 18 limitations.

Again, applicant's arguments are not found persuasive as it is the combination of references, which renders obvious said limitations of claim 18, see the instant Office Action stated above.

Applicant further argues that the Hogan reference does not teach the specific notification window that concomitantly displays items (a) and (b) recited in claim 18.

Again, applicant's arguments are not found persuasive as it is the combination of references, which renders obvious said limitations of claim 18, see the instant Office Action stated above.

The following rejection is being modified, which has been necessitated by amendment:

Claims 35-40, 44-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hogan (US A/N 2002/0110823) in view of Portwood et al. (US P/N 5,950,630) in view of Markin (US P/N 5,985,670) and further in view of Fey et al. (US 2002/0052761) as applied to claims 1-6, 11-14, 16, 18, 20-23, 27-31, and 33 above, and further in view of Classen (US P/N 6,219,674).

The combination of Hogan, Portwood et al., Markin, and Fey et al. teach claims 1 and 18 as described above and the limitations of claim 35, which overlap with claims 1 and 18 as discussed above in the instant office action.

With regards to amendments of claim 35: Hogan, Portwood et al., Markin, and Fey et al. suggest, but do not explicitly teach the amended claim step of:

"when the genetic test result value cannot be obtained, calculating the likelihood that the person displays a genetic mutation linked to the gene associated with the clinical agent based on genetic variability of the gene within the general population and constructing a message to communicate the calculated likelihood of the genetic mutation and any atypical clinical events that are associated therewith."

They suggest this because Hogan teaches an invention directed to a cost-effective way of determining risk of a patient for surgical complications. Hogan further teaches at paragraph [0013] the different factors are included in a genomic profile for determining the risk, such as information pertaining to differential diagnosis of recognized co-existing disease, information pertaining to pharmacokinetic and pharmacodynamic risks. Although Hogan's invention is directed to determining risk based on a genetic test result value, Hogan suggests using other information for said determination of risk as stated above. Furthermore, Hogan teach throughout the invention that the genomic profile information is communicated to a clinician, third party, or others for practical utilization.

Classen teaches at the abstract and cols. 1-5 storing adverse event data for drugs in a database. Classen teaches at col. 5- col. 6 that extracted data can be analyzed to calculate risk for an individual wherein the data of an individual is compared to the same persons with similar characteristics before receiving the medical product wherein these characteristics are applied to the general population, i.e. when

determining risk/benefit analysis for adults, the study would not include infants, it would use age to determine risk/benefit for similar aged populations. Classen teaches at col. 6, lines 13-17 wherein the characteristics are those such as race and genetic characteristics, which are applied to the general population. Therefore, the use of genetic characteristics from the general population in order to determine risk for an adverse event for a particular drug reads on calculating the likelihood that the person has a mutation linked to gene associated with the clinical agent based on the general population. Furthermore, Classen at Figs. 4-6 teach communicating said information to users, such as individuals, corporations, agencies, research institutions, health professionals, etc. Thus, Classen teaches constructing a message to communicate said risk assessment, i.e. likelihood of a genetic mutation and any atypical clinical event associated therewith.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used the database and methods for assessing risk based on general population data and construct a message to communicate said information as taught by Classen with the method taught by Hogan, Portwood et al., Markin, and Fey et al.. This is because Hogan teaches an invention directed to determining risk based on an obtained genomic profile. Hogan teaches calculating risk based on a genomic profile wherein the information is communicated to the clinician or other third party users. It would be implicit that if a genomic test result value cannot be obtained that other information would be used, such as population data wherein the information would be communicated to a third party as taught by Classen. Hogan teach at paragraph

[0006] that at-risk patients have been identified by a family history and at paragraph [0031] that other information has been used for calculating risk. It would have been obvious to one of ordinary skill in the art that when a genomic profile is not obtainable that determining risk of a patient based on other information can still be beneficial as taught by Hogan. Therefore, it would have been obvious to one of skill in the art to use an updated adverse event database populated with correlated general population data in order to determine risk when a genomic profile or genetic test result is not obtainable. The use of other information for determining risk was recognized as part of the ordinary capabilities of one skill in the art. One of ordinary skill in the art would have been capable of applying this known technique to the known method taught by Hogan, Portwood et al., Markin, and Fey et al. that was ready for improvement and the results would have been predictable to one of ordinary skill in the art.

Hogan at paragraphs [0005], [0008], and [0138] discusses assessing the dosages associated with the clinical agents and risk assessments as in claim 36.

Hogan at paragraphs [0186] and [0188] – [0193] discusses that the clinical agent and genetic information may be stored and communicated via various computerized applications, including electronic medical records including computers, which reads on claims 37 and 44.

Hogan at paragraph [0031] – [0033] discusses a problem is “how to alter treatment course of action in response to results,” as in genomic screening results and the present invention unites “medicine with genetics” to solve the described problem and to individualize treatment options for each subject. The genomic screening and

obtaining genomic profiles and Figs. 4 and 5 disclosed as examples of data sets comprising gene and allele associations with clinical agents implies a querying to determine if a gene is associated with a planned-to-be-administered clinical agent as in claims 38, and 39.

Hogan at paragraphs [0190] – [0191] teaches outputting information about the atypical clinical event associated with the polymorphism values such that a "clinical action" may be initiated as recited in claims 40 and 47.

Hogan at Fig. 4, discloses an example of a data set which includes information about risks associated with the atypical clinical events. Furthermore, at paragraphs [0115], [0129], [0136] – [0147], and [0186] teaches comparing genetic test result values for multiple genes to polymorphoism values associated with adverse reactions, i.e. risks associated with atypical clinical events, and that agent information may include dosage and other PK/PD parameters as in claims 46 and 50.

Hogan does not explicitly teach a method wherein the data sets of agent-gene associations may be updated as in claim 45.

Hogan at Fig. 2 describes in the analysis step of comparing genomic profile values to gene-agent association data that research data may be included in a data set used for comparison.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use data sets that may be updated. This is because it is a goal of Hogan's invention to tailor surgery treatments to subjects using genomic profiles and data, wherein it is implied that using the most updated genomic data available causes

the instant invention to be used in its most opportunistic way. Therefore, it is implied that the gene-agent association data sets used are data sets that are updated as is also the nature of research, to update the current information existing in the field.

Hogan does not explicitly teach a method wherein the data sets are incorporated into a single data set as in claim 48.

However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used combined data sets as it can be a more efficient means for comparing data and easier for visually comparing or looking up information such as gene-agent information. Furthermore, it is a common goal of researchers to consolidate the most updated information into single sources of data, wherein combining the most up to date information on gene-agent associations into a single source such as a single data set would be in line with research goals. Therefore, using a single source of data such as a single data set would be more efficient for determining risk assessments based on gene-agent associations.

Hogan at paragraph [0190] discusses that the risk assessment for the various treatment options are displayed to the clinician on a computer monitor, which reads on claim 49.

Response to Arguments

Applicant's arguments filed 2/26/2010 have been fully considered but they are not persuasive.

Applicant argues at pages 21-22 that Classen does not consider determining a genetic variability of a gene within a general population to ascertain whether to administer a test.

Applicant's arguments are not found persuasive as Classen at col. 5, lines 18-33 do suggest relating information to a individuals subgroups, such as age, gender, race, and/or other subgroups based on the vast amounts of information in the process of performing medical procedures. Furthermore, it is the combination of Classen with Hogan, Fey et al., Portwood, and Markin, which renders obvious said claim limitations.

Lastly, Applicant argues that the Hogan reference does not teach the recited limitation of claim 35 of "constructing a message."

Applicant's arguments are not found persuasive as Hogan reference is not used alone, but in combination with Fey et al., Portwood, and Markin for teaching said limitations, see the instant Office Action above.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jason Sims, whose telephone number is (571)-272-7540.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Marjorie Moran can be reached via telephone (571)-272-0720.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/ Jason Sims /

/Marjorie Moran/
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